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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,136	11/06/2006	David Wallach	30694/41887	3145

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EXAMINER	
WEN, SHARON X	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
10/06/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/573,136	WALLACH ET AL.	
	Examiner	Art Unit	
	SHARON WEN	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-19,26-36 and 45-61* is/are pending in the application.

5a) Of the above claim(s) *26-36 and 45-61* is/are withdrawn from consideration.

6)☒ Claim(s) *13* is/are allowed.

7)☒ Claim(s) *1-10,12 and 14-19* is/are rejected.

8)☒ Claim(s) *11* is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/01/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 09/01/2011 has been entered.

2. Applicant's amendment, filed 02/17/2011, has been entered.

Claims 20-25, 37-44 and 62-63 have been canceled.

Claims 1-19, 26-36 and 45-61 are pending.

Claims 26-36 and 45-61 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention/species, there being no allowable generic or linking claim.

Claims 1-19 are currently under examination as they read on an anti-NIK antibody that binds SEQ ID NO: 5, 6, and/or 3.

3. This Action will be in response to Applicant's Arguments/Remarks, filed 09/01/2011.

The rejections of record can be found in the previous Office Action, mailed 05/02/2011.

4. The previous rejections under 35 U.S.C. 102(e) as being anticipated by Schreiber et al. (US 6,822,138 B1) has been withdrawn in view of Applicant's amendment, filed 09/01/2011.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The previous rejection under 35 U.S.C. 103(a) as being unpatentable over Schreiber et al. (US 6,822,138 B1) in view of Green (*JIM* 1999 231:11-23) and Owens et al. (*JIM*, 1994, 168:149-165) has been withdrawn in view of Applicant's amendment, filed 09/01/2011.

8. Claims 1-10, 12, 14-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greene et al. (US Patent 6,265,538 B1) in view of Ferran et al. (US 2001/0053769), Campbell (*Monoclonal Antibody Technology*, 1984, Chapter 1, pages 1-32), Green (*JIM* 1999 231:11-23) and Owens et al. (*JIM*, 1994, 168:149-165).

The present claims are drawn to an anti-NIK antibody that binds specifically to an epitope comprising the phosphorylated threonine at position 559 (Thr-559).

Greene et al. taught the NIK polypeptide and that phosphorylation of NIK at Thr-559 is important in the activation of NIK being in the activation loop, amino acid positions 534-566 (which corresponds to SEQ ID NO: 6 of the instant application). Green et al. did not teach raising antibodies to the activation loop comprising phosphorylated Thr-559. However, it would have been obvious to one of ordinary skill in the art to make such antibody because: 1) making antibodies to a known antigenic target is a well-practiced technique in the art at the time of the invention was made as exemplified by Campbell (see entire document); and 2) there is a well-known need in the art to make and use specific antibodies that recognize the phosphorylated forms of NIK as exemplified by Ferran et al. (see entire document).

In particular, Campbell's taught that it is customary for any group working on a macromolecule to make monoclonal antibodies to it, *sometimes even without a clear objective for their application* (see Campbell, page 29, last paragraph). Given that Greene et al. taught the activation loop, aa 534-566, which is Applicant's SEQ ID NO: 6, it would have been obvious to one of ordinary skill in the art to make an antibody

targeting that fragment of NIK.

Moreover, the ordinary artisan would also have been motivated to make an antibody that specifically binds the above mentioned fragment of NIK only when Thr-559 contained in the fragment is phosphorylated because Ferran et al. expressly taught the desire to use such antibody that would specifically recognize the phosphorylated NIK to essay the kinase activity of NIK (see paragraph [0149]).

Given that Greene et al. taught Thr-559 is located in the activation loop and is one of the three phosphorylation sites responsible for the activation of NIK, and that Ferran taught using antibodies that specifically recognizes phosphorylated NIK to evaluate the activity of NIK; it would have been obvious to one of ordinary skill in the art to make an antibody that binds an epitope within the activation loop and comprises phosphorylated Thr-559.

The combined teachings particularly provide clear direction, motivation and expectation of success in making or using the antibodies that specifically recognize NIK only when it is phosphorylated at Thr-559. The ordinary artisan would arrive at the claimed invention based on reasons that flow logically from the teaching of the prior art.

Moreover, it would have been obvious to one of ordinary skill in the art to verify that the antibody only recognized Thr-559-phosphorylated NIK and does not bind unphosphorylated form because Ferran taught using antibodies that specifically recognize the phosphorylated form of the NIK. One of ordinary skill in the art would have been motivated to make an antibody against the activation loop of the NIK which contains the phosphorylated Thr-559 to study the molecule using common assays such as Western, ELISA and immunoprecipitation.

With respect to "human antibody", the following is noted.

The combined teachings of Greene and Ferran did not teach that the anti-NIK antibody is a human antibody. However it have been obvious to one of skill in the art at the time of the invention was made to make a human antibody against NIK because it was well-known in the art to make a human antibody as evidenced by Green (see entire document).

In particular, Green taught that XenoMouse strains of mice produced human monoclonal IgG antibodies (see, e.g., page 13-16, Section 2). Furthermore, Green taught that immunization of XenoMouse mice with human antigen *routinely* results in a robust secondary immune response, which can be ultimately captured as a large panel of antigen-specific fully human IgG mAb of sub-nanomolar affinity (see, e.g., Abstract). Moreover, one of ordinary skill in the art would also have been motivated to make the human anti-NIK antibodies because Green taught that monoclonal antibodies from XenoMouse animals have been shown to have therapeutic potential both in vitro and vivo (see, e.g., Abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to make the human anti-NIK antibody given that both the starting material, NIK antigen and the method of making human antibody with the antigen were both well-known in the art at the time of the invention was made.

With regard to "humanized or chimeric antibody or antibody fragments", the following is noted.

Although the combined teachings of Greene and Ferran did not teach the antibody to be humanized or chimeric, it would have been obvious to one of ordinary skill in the art at the time of the invention was made to generate a chimeric or humanized antibody against NIK because it is well-known in the art to make chimeric or humanized antibodies as evidenced by Owens et al. (see entire document, in particular, see pages 150-155).

In particular, Owens et al. taught the methods of humanizing rodent monoclonal antibodies by making human chimeric and human CDR-grafted antibodies from rodent monoclonal antibodies (see pages 150-155). Furthermore, Owen also taught the construction of antibody fragments such as Fv and scFv (see page 155).

One of ordinary skill in the art would have been motivated to make a chimeric or humanized antibody against NIK and the antibody fragments as taught by Schreiber et al. because antibodies can be used for therapeutic purposes and that making a rodent monoclonal antibody chimeric or humanized is advantageous to the rodent monoclonal

antibody for human diagnosis or therapy as taught by Owens (see Introduction). Moreover, using antibody fragment has the advantage of faster clearance from the body. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to make an antibody that binds and antagonizes NIK wherein the antibody is chimeric or humanized, as well as an antibody fragment.

Given the above discussion, the invention, as a whole, was *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

9. Claim 13 is allowed.
Claim 11 is objected.
Claims 1-10, 12, 14-19 have been rejected.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571)272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/
Primary Examiner, Art Unit 1644